

## **DETAILED ACTION**

### ***Response to Amendment/ Arguments***

Applicants' amendments filed April 21, 2010 amending claim 11 and canceling claims 16, 19, 22 and 23 have been entered. Claims 1-10, 12-15, 20, 21 and 35 were previously canceled. Claims 11, 17, 18 and 24-34 are currently pending.

Due to Applicants' amendment to the claims, the previous rejections under 35 USC 103 are withdrawn. Applicants have filed a terminal disclaimer over U.S. Patent No. 7,700,122 obviating a rejection of claims 27-34 under obviousness-type double patenting over claims 1-13 of U.S. Patent No. 7,700,122. As such claims 11, 17, 18 and 24-34 are free of the art and allowable following the Examiner's Amendment detailed below.

## **EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mark Russett on May 26, 2010.

The application has been amended as follows:

(1) Claim 27:

DELETE "or preventing" from line 2.

(2) Claim 34:

DELETE "prevent or" from line 3.

### **Examiner's Statement of Reasons for Allowance**

The following is an examiner's statement of reasons for allowance:

Claims 11, 17, 18 and 24-34 of the instant application claim a method of providing topical analgesia to a subject comprising the topical administration to peripheral sites a pharmaceutical composition comprising morphine and butamben in a ratio of about 1:0.4.

The closest prior art is Elkhoury et al. U.S. Patent No. 5,589,480 in view of Elden U.S. Patent No. 5,814,659 and further in view Saito et al. (1998, Anesthesiology, Volume 89(6), pages 1455-1463).

Elkhoury et al. teach the topical administration of an opioid drug, such as morphine, to produce an analgesic effect in a localized peripheral area and without a transdermal migration of the opioid drug into the blood stream (see Abstract). Elden teaches topical analgesic compositions and methods for inducing topical analgesia (see abstract).

Although it would be obvious to combine morphine and butamben in a topical composition since both drugs are useful for the same purpose, Applicants have presented a showing of unexpected results wherein morphine and butamben combined

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in a ratio of 1:0.4 produces a synergistic interaction which could not have been predicted.

In addition, lidocaine and butamben are both local anesthetics with similar mechanisms of action. Saito et al. teach that morphine and lidocaine have a synergistic antinociceptive interaction in both bolus injections and in continuous coinfusion in which the agents are administered in small volumes and low concentrations.

However, although morphine and lidocaine are known to have synergistic interactions, due to the unpredictability of the art, an ordinary skilled artisan could not have predicted that morphine and butamben would also have synergistic interactions since lidocaine and butamben are different compounds. Furthermore Saito et al. teach a synergistic interaction when morphine and lidocaine are administered by injection and not when administered topically.

Thus, the recited claims if the instant application are novel and non-obvious over the closest prior art references.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

***Conclusions***

Claims 11, 17, 18 and 24-34 are allowed. Claims 1-10, 12-16, 19-23 and 35 are canceled.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARA R. MCMILLIAN whose telephone number is (571)270-5236. The examiner can normally be reached on Monday-Thursday from 8:30 am- 6:00 pm and every other Friday from 8:30 am- 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kara R. McMillian/  
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Supervisory Patent Examiner, Art Unit 1627